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Paper 418
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UNITED STATES PATENT AND TRADEMARK OFFICE
BOARD OF PATENT APPEALS AND INTERFERENCES

Patent Interference 105,592 McK
Technology Center 1600

CENTOCOR, INC.
(Inventors: Jill Giles-Komar *et al.*)

Application 10/912,994,
Junior Party,

v.

ABBOTT GmbH & CO., KG,
(Inventors: Jochen Salfeld *et al.*)

Patent 6,914,128,
Senior Party,

Before: FRED E. McKELVEY, *Senior Administrative Patent Judge,* and RICHARD E. SCHAFER and SALLY GARDNER LANE, *Administrative Patent Judges.*

McKELVEY, *Senior Administrative Patent Judge.*

MEMORANDUM OPINION
Decision on Centocor Motion 1 and Abbott Motion 1

A. Why both motions are being considered on the merits

The time: 12 noon.

The date: 5 July 2005

The event: Issuance of Abbott U.S. Patent, 6,914,128 B1.

The place: Abbott's patent department, where excitement was in the air.

A research project which began in July of 1993 had finally resulted in a patent.

The excitement was short-lived.

It turned out that Centocor had a patent application pending claiming the "same patentable invention."

Centocor managed to talk the Examiner into recommending and the Board into declaring an interference.

Any disinterested observer will immediately appreciate the fact that declaration of the interference put sand in Abbott's patent gears.

Looking at the big picture, on previous occasions Abbott and Centocor have been on the same side.

An example is a civil action by my state against both of them along with a bunch of others. *Hawaii v. Abbott Laboratories, Inc.*, 469 F. Supp.2d 835 (D. Hawaii 2006).

While they may have been on the same side in 2006, one gets the impression that lately Abbott and Centocor don't get along when it comes to the market place. *Centocor Ortho Biotech, Inc. v. Abbott Laboratories*, 2009 WL 1473431 (E.D. Tex May 27, 2009, as amended May 29, 2009) and 2009 WL 938703 (E.D. Tex Apr. 6, 2009).

Recent news is not good for Abbott.

Apparently, the S.D. Tex. has entered a judgment for Centocor and against Abbott for $1.67 *billion* (not million). See *J&J Wins Record $1.67 Billion Verdict From Abbott* reported at

http://www.bloomberg.com/apps/news?pid=email_en&sid=a0h5zEnztLs0

(6 July 2009).

We suspect that the Federal Circuit will be asked to look into the judgment.

Getting back to the interference, the Board has authority to resolve priority and patentability issues.

We have already resolved Abbott Motion 7. Paper 417.

No doubt there will be renewed excitement at Abbott over the outcome of Abbott Motion 7.

But, it turns out that even if Abbott prevails on priority, Centocor tells us (and Abbott) via Centocor Motion 1 that Abbott's involved patent claims are unpatentable.

Abbott tells us (and Centocor) via Abbott Motion 1 that Centocor's involved claim 1 is not patentable over the art.

Having prevailed on priority, Abbott says we should *not* get to the issue of patentability because Centocor is *not* the first inventor.

By deciding the Abbott priority motion, Abbott reasons that we have answered any question the Examiner may have about issuing an application to Centocor with claims corresponding to what is now a lost count—in other words, the Examiner can now examine the Centocor application.

Centocor says that case of unpatentability over the art case has been developed and, we need to go ahead and decide the patentability.

At oral argument on 30 June 2009, the pros and cons of deciding the patentability were debated at great length.

We agree with Centocor and exercise our discretion (the statute says we "may" consider patentability) and decide Centocor Motion 1.

The Examiner cannot get into patentability of the Abbott patent unless a reexamination is requested.

Abbott is not likely to file a request for reexamination.

Centocor does not like the notion of any ex parte and inter partes reexaminations because institution of a reexamination would start the whole process over and delays an eventual ruling on the patentability of Abbott's claims.

We have the arguments and evidence of patentability before us.

As a result, it makes sense in this particular case to decide patentability.

A ruling on patentability—at least in this case—will help Abbott and Centocor executives to plan future business activates.

Our decision to look into patentability is consistent with, albeit it not dictated, by *Perkins v. Kwon*, 886 F.2d 325 (Fed. Cir. 1989).

We also decide Abbott Motion 1.

B. Introduction

The interference is before a merits panel for consideration of priority and other issues.

One of the other issues, is Centocor Motion 1 which seeks judgment against the involved Abbott claims based on alleged unpatentability of those claims under 35 U.S.C. § 103.

Centocor has not taken the position that its claims are patentable if the Abbott claims are unpatentable. Accordingly, involved Centocor claims 1, 102 and 103 stand or fall with the decision on whether the Abbott claims are unpatentable on the merits under 35 U.S.C. § 103. See 37 C.F.R. § 41.207(c) (2008).

Another issue is Abbott Motion 1 which maintains that involved Centocor claim 1 is unpatentable over the art.

Centocor motion for judgment based on obviousness

Centocor filed Centocor Motion 1 for judgment based on alleged unpatentability under 35 U.S.C. § 103 over the prior art. Paper 34.

Abbott opposed. Paper 89.

Centocor replied. Paper 119.

Abbott motion for judgment based on the prior art

Abbott filed Abbott Motion 1 for judgment based on alleged unpatentability of involved Centocor claim 1 (but not involved Centocor claims 102 or 103) as being unpatentable over the prior art. Paper 35; see also Paper 36.

Centocor opposed. Paper 90.

Abbott relied. Paper 121.

The motion was deferred to the priority phase. Paper 127.

B. Abbreviations

The following abbreviations are used in this opinion.

CDR	Complimentary determining regions (Ex 2040, page 60:16-17)
HBV	Hepatitis B virus
HIV	Human immunodeficiency virus
PRC	Polymerase chain reaction

C. Abbott Motion 1

Abbott Motion 1 maintains that involved Centocor claim 1 is unpatentable under 35 U.S.C. § 102, and alternatively under 35 U.S.C. § 103. Paper 35; see also Paper 36. Abbott Motion 1 does not address involved Centocor claims 102 and 103.

We need not spend a lot of time on Abbott Motion 1.

It fails to state a claim for relief.

A review of the motion immediately establishes that Abbott has not undertaken to prove, or that it has made out, its case on the merits.

Abbott's case for relief goes something like this.

Abbott's original claim 1 read as follows (Ex 2013, page 145):

> An isolated human antibody, or an antigen-binding portion thereof, that binds to IL-12, wherein the human antibody is a neutralizing body.

The similarity between Abbott's original claim 1 and Centocor claim 1 is apparent.

Centocor claim 1 reads as follows (Paper 5):

> An isolated human antibody, or an antigen-binding portion thereof, that binds to human IL-12, wherein said human antibody is a neutralizing antibody.

The difference is that Abbott uses the phrase "*the* human antibody" whereas Centocor uses the phrase "*said* human antibody."

During pendency of the Abbott non-provisional application which matured into the involved Abbott patent, the Examiner rejected original Abbott claim 1 over the prior art. Ex 2011 (the same exhibit as Ex 1008), page 10.

The prior art cited by the Examiner was Trinchieri, U.S. Patent 5,811,523 (Ex 2001).

Upon filing of a response to the Examiner's rejection, Abbott folded. It cancelled original claim 1. Ex 2012, page 2.

In place of original claim 1, Abbott amended claim 8 to recite additional limitations (shown in italics below):

> An isolated human antibody, or antigen-binding portion thereof, that binds to human IL-12 and *dissociates from human IL-12*

with a K_d of 1 x 10^{-10} M or less and a k_{off} rate constant of 1 x 10^{-3} s^{-1} or less, as determined by surface plasmon resonance.

The portion in italics replaced the "a neutralizing antibody" of original claim 1 and further limits the antibody of original claim 1 to an antibody having a particular degree of neutralization.

The Examiner agreed amended claim 8 was allowable and a patent issued.

Claim 8 of the Abbott non-provisional application, upon renumbering—a standard procedure in the USPTO upon allowance of an application—became claim 1 of the Abbott patent.

During examination of the Centocor application, the Examiner did not apply the Trinchieri patent—Abbott would say because Centocor did not get around to citing the patent to the Examiner until late in the prosecution.

Late citing and related issues involving alleged shenanigans on the part of Centocor have been disposed of via our decision on Abbott Motion 3. Paper 184, rehearing denied, Paper 191.

Abbott's proofs of the alleged unpatentability of Centocor claim 1 are based on the Examiner's rejection in the Abbott application—not a rejection of claim 1 of the Centocor application.

Abbott's reasoning is that if the Examiner felt Abbott original claim 1 was anticipated by Trinchieri, then surely the Examiner has to feel that Centocor claim 1 is unpatentable over Trinchieri.

Another way of looking at it is that if Abbott's claim 1 is unpatentable over Trinchieri, then Centocor's claim 1 is also unpatentable over Trinchieri.

It is true that Abbott surrendered the subject matter of Abbott original claim 1 upon cancellation of original claim 1. But, we are not evaluating a

recapture rejection or a *doctrine of equivalents* surrender issue in an infringement context.

The initial decision by the Examiner to reject Abbott original claim 1 in no way binds Centocor. *Sze v. Bloch*, 59 CCPA 983, 987, 458 F.2d 137, 140 (CCPA 1972) (holding during ex parte examination cannot be binding in subsequent inter partes case involving application in which holding was made); *Switzer v. Sockman*, 52 CCPA 759, 333 F.2d 935 (CCPA 1964). If higher authority is needed, see *Keystone Bridge Co. v. Phoenix Iron Co.*, 5 Otto (95 U.S.) 274, 279 (1877) (patents are procured *ex parte*; the public is not bound by decision of the Patent Office to issue the patent, but a patentee is). Nor does the Examiner's decision to reject, or not reject, bind us. *Glaxo Wellcome Inc. v. Cabilly*, 56 USPQ2d 1983 (Bd. Pat. App. & Int. 2000)

We do not know what the Examiner would have done during prosecution of the Abbott non-provisional application had Abbott argued that the rejection of original Abbott claim 1 over Trinchieri was erroneous.

As indicated above, Abbott avoided that battle by cancelling claim 1.

What we do know is that the Examiner did *not* reject a claim essentially the same as Abbott original claim 1 when it came to prosecution of the Centocor application.

Our rules require that a moving party explain why it is entitled to relief. 37 C.F.R. § 41.121(c)(1)(iii) (2008).

Abbott does not propose findings or explain *on the merits* why Centocor claim 1 is unpatentable over Trinchieri. What the Examiner did or did not do does not establish for Abbott why involved Centocor claim 1 is unpatentable over Trinchieri.

Rather, Abbott tries to back door the matter by saying the Examiner held my claim 1 to be unpatentable over Trinchieri and therefore Centocor's claim 1 has to be unpatentable over Trinchieri.

Abbott's position fails to state a claim for relief.

On that basis, we deny Abbott Motion 1.

D. Centocor Motion 1

1. Technical background

For a tutorial background, we reproduce some of the material set out in our decision on Abbott Motion 7.

Interleukin **12**—known as IL-12—is a protein made in the body by humans. Paper 405, page 4; Centocor, page 1.

In biotechese, IL-12 is referred to as a "cytokine."

IL-12 is a useful protein unless—as Yogi Berra would say—it is not a useful protein.

IL-12 plays a role in immune response.

In other words, when foreign material invades the body, IL-12 might be released as part of the body's immune response.

In biotechese, the foreign material is known as an "antigen" (from "**anti**body **gen**erating substances")

Unfortunately, IL-12 can be overproduced in the body (or as Abbott states "deregulated"—Paper 405, page 4) and then become what might be referred to as a "self-antigen."

Overproduction is not a good thing and is said to lead to such immune diseases as rheumatoid arthritis, psoriasis and Crohn's disease—to name a few. Paper 409, page 1.

When overproduction occurs, one way to bring IL-12 back into a "useful" role is to "tie" some of it up so that less IL-12 is available.

Both parties have discovered that one way to do "tie" up excess IL-12 is to bind at least some of it with an antibody.

Key to the discovery, is that the antibody be a "human antibody" (as opposed to say a "mouse antibody").

Not only does the antibody have to "bind" to IL-12, but it must also "neutralize" IL-12.

The diagram below, provided by Centocor (Paper 409, page 2), shows one antigen bound to an antibody.

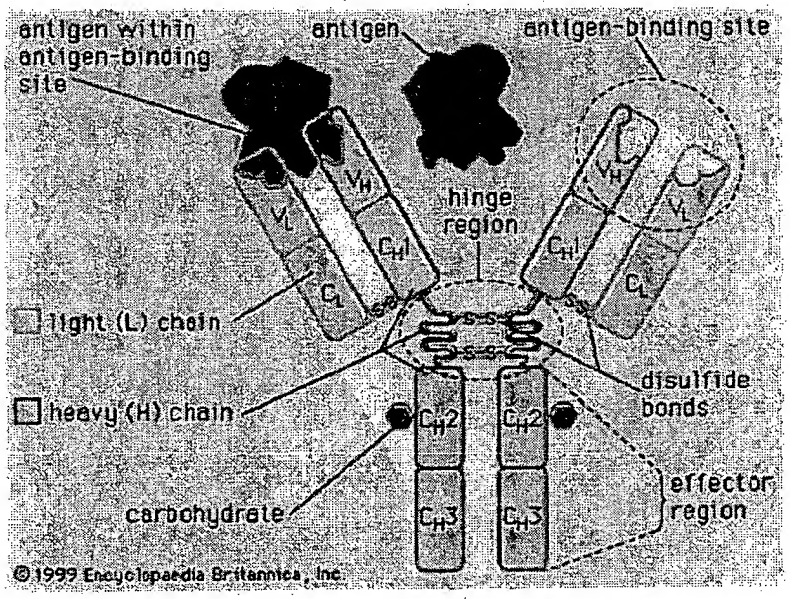

Fig. 1

Schematically depicted is a antigen bound to an antibody

As can be seen from the diagram, there are two antigens (the irregular shaped black objects). The antibody is shown as a generally Y-shaped object. One of the antigens (i.e., IL-12) is shown bound to the antibody. The other is shown floating around and is not bound to the antibody.

Whether the antigen is sufficiently bound to the antibody depends on the strength of interaction between the antigen and antibody. Paper 409,

page 4. The rate of binding of antigen and antibody at a particular concentration is a constant identified as k_{on}. Another constant (k_{off}) is the rate at which the antigen dissociates from the antibody. Paper 409, page 4. Centocor explains as follows (Paper 409, pages 4-5):

> a typical antigen-antibody binding and dissociation can simply be represented as follows:

$$\text{Antibody} + \text{Antigen} \underset{k_{off}}{\overset{k_{on}}{\rightleftharpoons}} \text{Antibody-Antigen}$$

> Equilibrium is reached when the rate at which new antigen-antibody complexes are formed equals the rate at which the antigen-antibody complexes dissociate. At equilibrium:
> [Antigen][Antibody]$\cdot k_{on}$ = [Antigen-Antibody] $\cdot k_{off}$
> K_d is a value that describes the relative relationship of k_{off} and k_{on} when the reaction is at equilibrium.

$$k_{off} / k_{on} = K_d$$

In a footnote (Paper 409, page 5 n.1), Centocor explains:

> [Antigen] is a notation for the concentration of Antigen; likewise, the notation [Antibody] refers to the concentration of the Antibody. [Antigen-Antibody] refers to the concentration of the antigen-antibody complex.

The parties tell us that there are various ways to measure antibody-antigen affinities. According to Centocor, one method is using Surface Plasmon Resonance (SPR). Paper 409, pages 5-7. According to Abbott, another method is via Receptor Binding Assay (RBA). Paper 405, pages

11-12. Yet another method according to Abbott is via PHA Blast Neutralization Assay (PHA). Paper 405, pages 12-13.

E. Centocor's obviousness case--facts

To the extent a sentence is a finding of fact, we believe the finding is supported by a preponderance of the evidence.

To the extent a sentence is a conclusion of law, it may be treated as such.

1. O'Neil testimony

O'Neil's background

Centocor's obviousness story emerges from the testimony of Dr. Karyn T. O'Neil (Ex 2015), previously known as K. F. Thompson (Ex 1089, page 239:8-9).

O'Neil is an employee of Centocor. Ex 2015. ¶ 1.

O'Neil has a 1998 Ph.D. from the University of Pennsylvania. Ex 2015, ¶ 1.

O'Neil has been involved with the creation and use of antibody libraries, including phage display libraries, for selection and engineering of antibodies for ten years. Ex 2015, ¶ 2:13-15.

The O'Neil declaration was signed in 2008; so "for ten years" means since 1998.

During the ten years, O'Neil had extensive experience characterizing and measuring the activity of various proteins, including administering assays measuring IC_{50}. Ex 2015, ¶ 2:16-18.

O'Neil says that she is qualified to state the facts and opinions set forth in her testimony. Ex 2015, ¶ 2:18-19.

O'Neil has read Abbott Patent 6,914,128 and says she is familiar with its contents. Ex 2015, ¶ 3.

O'Neil goes on to describe (1) antibodies, (2) heavy chains, (3) light chains, (4) immunoglobulin diversity, (5) somatic hypermutation and affinity maturation, (6) laboratory production of antibodies, (7) recombinant antibodies, (8) chimeric and humanized antibodies, (9) fully human antibodies, (10) (IL-12, (11) IC_{50} and (12) K_d, k_{on} and k_{off}. Ex 2015, ¶¶ 5-22.

O'Neil testified on direct as follows (Ex 2015, ¶ 15):

> On challenge faced in therapeutic use of monoclonal antibodies is the use of mouse or other rodent antibodies in humans. Although, for example, murine antibodies can have significant structural similarity to human antibodies, there are differences in their sequences and thus their structures. The human immune system recognizes mouse antibodies as foreign, and a process referred to as HAMA (human antibodies to mouse antibodies) rapidly removes them [i.e, the mouse antibodies,] from circulation, causing systemic inflammatory effects. A solution to this problem [i.e., problems caused through use of mouse antibodies in humans,] would be to generate human antibodies directly from humans. However, this [i.e., generation of human antibodies directly from humans,] is not easy, primarily because it is generally not seen as feasible to challenge humans with antigen in order to produce antibody. Furthermore, due to immune tolerance issues, it is not easy to generate human antibodies against human tissue.

See also Ex 1089, page 199:7-18 (O'Neil cross).

O'Neil next walks the Board through various claims in the Abbott patent. Ex 2015, ¶¶ 25-34.

There follows a discussion about the prosecution history of the application which matured into the Abbott patent. Ex 2015, ¶¶ 35-40.

Prior art relied upon by Centocor

O'Neil eventually reaches the prior art which Centocor says renders obvious the subject matter of the involved Abbott claims.

The prior art relied upon by Centocor is:

Name	Identification	Date	Exhibit Number
Trinchieri	U.S. Patent 5,811,523	22 Oct 1997	2001

Valiante	145 *Cell. Immunol.*, pages 187-198: Role of the Production of Natural Killer Cell Stimulatory Factor (NKSF/IL-12) in the Ability of B Cell Lines to Stimulate T and NK Cell Proliferation	1992	2002
Chizzonite	147 J. Immunol., pages 1548-56: IL-12: Monoclonal Antibodies Specific for the 40-kDa subunit Block Receptor Binding and Biologic Activity on Activated Human Lymphoblasts	1991	2003
Gately	U.S. Patent 5,780,597	14 Jul 1998	2004
Queen	U.S. Patent 5,530,101	19 Dec 1990	2005
Burton	U.S. Patent 5,652,138	19 July 1994	2006
Curiel	U.S. Patent 5,910,486	6 Jun 1995	2007

Tomlinson	256 J. Mo. Biol., pages 813-17, The Imprint of Somatic Hypermutation on the Repertoire of Human Germline V Genes	1996	2008
Hoogenboom	15 Trends in Biotechnology, pages 62-70	1997	2009

Abbott does not contest the prior art status of any of the nine prior art references relied upon by Centocor.

Basis for alleged unpatentability over the prior art

According to Centocor, involved Abbott claims 1-15, 27-40 and 50-64 are unpatentable under 35 U.S.C. § 103 over (1) Valiante, (2) Chizzonite and/or (3) Gately further in view of (4) Queen, (5) Burton, (6) Curiel, (7) Tomlinson and (8) Hoogenboom. Paper 34, page 18.

Further according to Centocor, involved Abbott claims 1-15, 27-40 and 50-64 are unpatentable under 35 U.S.C. § 103 over (1) Trinchieri, (2) Curiel, (3) Tomlinson and (4) Hoogenboom. Paper 34, page 19.

Trinchieri

According to O'Neil, Trinchieri describes "the complete human IL-12 protein." Ex 2015, ¶ 41 (O'Neil direct); Ex 1089, page 133:10 to 134:12 (O'Neill cross); Ex 2001, col. 2:27-31 and Figs. 1A-1D.

O'Neil testified on direct that Trinchieri claims "a neutralizing human antibody to human IL-12." Ex 2015, page 12:1; Ex 2001, col. 22, claim 5 ("The antibody of claim 1 wherein said antibody is a human antibody."). On

cross, O'Neil backed off and conceded that Trinchieri claim 5 is not to a "neutralizing" antibody. Ex 1089, page 135:4-13. *See also* Ex 1089, page 150:9-15.

Valiante

Valiante is said to describe (1) human IL-12, the p40 and p35 chains of IL-12, (2) recombinant production of IL-12 and (3) *murine* antibodies to human IL-12. Ex 2015, ¶42.

The anti-IL-12 "antibody 8.6" described in Valiante contains the subclone "Antibody 8.6.2" said to be described and used in the Examples of the Abbott patent. Ex 2015, ¶ 42:11-13. O'Neil does not have first-hand knowledge of what Abbott *used* in its examples. Neither party attempted to prove what Abbott *used.* From a prior art point of view, what counts is what Valiante *describes*. *Joy Technologies, Inc. v. Manbeck*, 751 F. Supp. 225, 233 n.2 (D.C.C. 1990) (Fed. Cir. Judge Bennett—sitting by designation).

According to O'Neil, "Antibody 8.6" is shown in Valiante to be a neutralizing antibody by its described effect on reducing the effect of IL-12 in cell cultures. Ex 2015, ¶ 42:14-15; Ex 2002, pages 191-195.

On cross, O'Neil agreed that Valiante did not describe *human* antibodies to human IL-12. Ex 1089, page 152:5-7.

Chizzonite

Chizzonite is said to describe at least (1) human IL-12 and (2) production of *rat* antibodies to human IL-12, and (3) specifically the p40 subunit of IL-12. Ex 2015, ¶ 43; Ex 2003, pages 1548, 1553 and 1554

According to O'Neil, Chizzonite characterizes two classes of antibodies: (1) inhibitory antibodies that neutralize IL-12 bioactivity and (2) noninhibitory antibodies that bind to IL-12 without neutralizing bioactivity. Ex 2015, ¶ 43:18-20; Ex 2003, pages 1548-49.

Further according to O'Neil, Chizzonite describes neutralizing antibodies that impact IL-12 bioactivity. Ex 2015, ¶ 43:21-22; Ex 2003, page 1553.

On cross, O'Neil agreed that Chizzonite does not describe *human* antibodies to human IL-12. Ex 1089, page 154:23-25.

Gately

Gately is said to describe (1) human IL-12, (2) its p40 and p35 chains and (3) its bioactivity. Ex 2015, ¶ 44; Ex 2004, Examples 2-9.

Gately is further said to describe isolation and purification techniques for obtaining IL-12. Ex 2015, ¶ 44:25-26; Ex 2004, Example 1.

Gately is still further said to describe specific *non-human* antibodies that are said to neutralize bioactivity of IL-12. Ex 2015, ¶ 44, 26-27; Ex 2004, Example 9 (O'Neil refers to Example 39, but there is no Example 39; we believe she was referring to Example 9).

On cross, O'Neil agreed that Gately does not describe human antibodies to human IL-12. Ex 1089, page 157:25 to page 158:3.

Queen

Queen is said to describe methods for producing humanized antibodies from a non-human donor antibody. Ex 2015, ¶ 45; Ex 2005, col. 11:55-58.

Reference is made to chimeric antibodies. We understand a chimeric antibody to be one which contains both (1) human portions and (2) non-human portions. *See, e.g.*, Ex 2015, ¶ 20:26.

Queen is said to reveal that non-human antibodies had potential problem when used in humans and therefore human antibodies were desirable. Ex 2015, ¶ 46; Ex 2005, col. 1:33 to col. 2:23.

Specifically, Queen states (Ex 2005, col. 1:41-47) (bold in original):

> Perhaps most importantly, non-human monoclonal antibodies contain substantial stretches of amino acid sequences that will **be-immunogenic when injected into a human patient.** Numerous studies have shown that after injection of a foreign antibody, the immune response mounted by a patient can be quite strong, **essentially eliminating the antibody's therapeutic utility after an initial treatment.**

Putting aside numerous parent applications, Queen was filed in 1990 as a continuation-in-part of earlier applications. The earlier applications are not in evidence. In a light most favorable to Centocor, we view Queen as saying that in 1990 the pharmaceutical industry had a reason and motivation to "come up" with a non-chimeric (i.e., fully human) antibody which hopefully would not be "rejected" by the human body after injection.

On cross, O'Neil agreed that Queen describes method for producing humanized antibodies from a non-human donor antibody. Ex 1089, page 160:3-7.

Nevertheless, O'Neil maintained that Queen might describe a human antibody. Why? On cross, the following occurred (Ex 1089, page 167:4-8):

> Q. Okay. Do any of the steps referred to in Queen result in a human antibody?
>
> A. I think that would depend in the end on the percent homology identity to human antibody genes.

A fully human antibody is made from a human source. What O'Neil means by "homology" is that if

> (1) an antibody is "mostly" (our word) made up of human material, but

(2) happens to have a minor amount of non-human (say mouse) material where the mouse material sequence looks a lot like (say 80% like) the corresponding human material sequence the mouse sequence replaces, then

(3) the antibody is a human antibody.

In other words, in O'Neil's opinion a "mostly human antibody" is a "human antibody" even if a minor portion of the mostly human antibody comes from, say, a mouse. We will have more to say about O'Neil's view vis-à-vis what Abbott says in its patent later in this opinion.

Burton

Burton is said to reveal that as far back as 1991 various techniques had been developed for (1) selecting human antibodies to an antigen and (2) humanizing non-human antibodies—in particular via a "phage display technique. Ex 2015, ¶ 48.

According to O'Neil, Burton describes the use of a phage display technique to generate human antibodies to hepatitis B virus (HBV) and HIV. Ex 2015, ¶ 48, page 13:27 through page 14:2.

O'Neil then takes us through an analysis of Burton discussing the steps one would take to make human antibody to IL-12 and how use of those steps "will enable selection of higher affinity binders." Ex 2015, ¶¶ 49-53.

At the root of O'Neil's analysis is a belief that in March of 1999 all one of ordinary skill in the art would need to do in order to find a human antibody to human IL-12 would be carry out the steps of ¶¶ 50-52 of her declaration until a desired affinity was achieved. Ex 1089, page 195:18 through page 196:10.

Thus, in O'Neil's opinion, Burton provides the recipe for making human antibody to human IL-12—an objective which would have been predictable.

Curiel

Curiel is said to show that by 1994 "kits" and reagents for generating phage display libraries were available. Ex 2015, ¶ 54; Ex 2007, col. 7:21-25.

Curiel is further said to show that once these kits or methods are used to produce an antibody library on the surface of a display package (e.g., a phage), the antibody library is screened with a protein of interest to identify and isolate packages that express an antibody that binds to the antigen of interest. Ex 2015, ¶ 54:24-27; Ex 2007, col. 7:51-53.

Display packages expressing antibodies that bind immobilized antigens can then be selected. Ex 2015, ¶ 54, page 16:1-2.

Despite her testimony concerning Curiel "kits," O'Neil indicates that (1) she has no hands-on experience with kits (Ex 1089, page 203:2-3) and (2) she never used "these kits" (Ex 1089, page 204:15-16 and page 207:6-7).

Tomlinson

Tomlinson is said to describe the mechanism of antibody binding was "well-understood in the art prior to the Abbott patent." Ex 2015, ¶ 58.

Tomlinson is also said to describe how it was well known that the antibody contained regions that bound to the antigen through specific protein-protein interactions. Ex 2015, ¶ 58:23-25.

An antibody bound to an antigen is shown in Fig. 1 of this opinion.

Hoogenboom

Hoogenboom is said to describe the use and generation of phage display libraries and selection strategies for generating high-affinity antibodies. Ex 2015, ¶ 59; Ex 2009.

As O'Neil explains, techniques described by Hoogenboom are said to allow for human antibodies to be created that bind to a chosen antigen. Ex 2015, ¶ 60.

In addition, the techniques allow for improving binding affinity of these antibodies. Ex 2015, ¶ 60:6.

Additional prior art comment

According to O'Neil, many of the values recited in Abbott's claims are similar to or less stringent than values described in the Abbott patent for prior art antibodies. Ex 2015, ¶ 63.

On cross, O'Neil explains what she means by "many of the values" and "values described" but ultimately agrees that the prior art antibodies said to have been described by Abbott are *not* human antibodies. Ex 1089, page 218:15-17.

Level of skill in the art—O'Neil

On direct, O'Neil testified that in March of 1999 a person having ordinary skill in the art would have a Ph.D. in microbiology "or a similar degree." Ex 2015, ¶ 65.

On cross, O'Neil backtracks and indicates that she does not think it absolutely essential that one have a Ph.D. Ex 1089, page 89:18-20.

Apparently, someone with the experience of a Ph.D. in terms of laboratory skill would be skilled in the art. Ex 1089, page 90:9-12.

In addition, the "person" would have four years of experience making, modifying and testing antibodies. Ex 2015, ¶ 65:2. On cross, O'Neil

explains that four years "is about a reasonable timeframe for that, and so that being the first couple of years of your Ph.D. you're probably not doing an enormous amount of hands-on things ..." Ex 1089, page 89:11-18.

We have said in past cases that identifying a degree and years of experience is not helpful. *Argyropoulos v. Swarup*, 56 USPQ2d 1795, 1807 (Bd. Pat. App. & Int. 2000) (explaining why defining the level of skill in the art in terms of degrees obtained is less helpful than defining it in terms of what such a person would have known and what the person would have been able to do). Abbott's cross-examination of O'Neil more than proves our point.

Back to the level of skill, O'Neil tells us that persons of ordinary skill in "this art" keep abreast of the literature and routinely apply scientific discoveries to practical uses. Ex 2015, ¶ 65:3:4.

The level of skill "was and is very high." Ex 2015, ¶ 65:5.

One skilled in the art would have been very familiar with the techniques for (1) obtaining non-human antibodies for a known antigen, (2) humanizing non-human antibodies and (3) improving the affinity of antibody. Ex 2015, ¶ 65:6-8.

One skilled in the art would have known of the desirability of achieving human antibodies with the Abbott claimed values (i.e., K_d and k_{off}). Ex 2015, ¶ 64. How would one skilled in the art obtain the claimed values? By using (1) well-known humanization and affinity maturation methods and phage display selection techniques, (2) generating human antibodies having the claimed values "and/or" (3) improving the affinity of prior art antibodies in order to achieve the claimed values—all said by O'Neil to be "well within" the skill of the art in 1999. Ex 2015, ¶ 64:22-26

(direct); Ex 1089, page 219:6 to page 220:22. At this point, one plausibly might wonder if O'Neil forgot that portion of her direct where she states:

> However, this [i.e., generation of human antibodies directly from humans,] is not easy, primarily because it is generally not seen as feasible to challenge humans with antigen in order to produce antibody. Furthermore, due to immune tolerance issues, it is not easy to generate human antibodies against human tissue.

Ex 2015, ¶ 15.

Obviousness analysis—O'Neil

The problem was to obtain human antibodies with characteristics comparable to prior art non-human anti-IL-12 antibodies. Ex 2015, ¶ 80. When asked on cross, where the problem was identified, O'Neil answered that she did not "know the answer to that." Ex 1089, page 225:19-20.

Those skilled in the art had a limited number of available methodologies to obtain the antibody. Ex 2015, ¶ 80:11-12.

The person of ordinary skill would have had reason to pursue the small number of methodologies. Ex 2015, ¶ 80:12-17.

Quoting from *KSR*, O'Neil appears to assume the role of patent attorney and tells us that obtaining an antibody with the characteristics of Abbott's involved claims was "the product not of innovation but of ordinary skill and common sense." Ex 2015, ¶ 80:17-18.

O'Neil was asked whether there would be "a reasonable expectation that the techniques would be successful" (Ex 1089, page 226:6-7). She agreed that there would have been a substantial amount of work. A high amount of work could be achieved says O'Neil depending "on how many people you have working on it." Ex 1089, page 226:23-24. "There [would

have been] ... a fairly high expectation of success." Ex 1089, page 227:1. There was a "high probability of success." Ex 1089, page 227:20-21. High probability? Yes. Ex 1089, page 227:22-23. How high? "I would go into it assuming that I was going to be successful, and I think most people at that point in time would also do that." Ex 1089, page 227:25 to page 228:4. So, says O'Neil, "predictability is related to whether it's anticipated that you will be able to identify the antibody that you're looking for." Ex 1089, page 228:15-18.

2. Iverson testimony

The first—Centocor—to present his case seems right, till another—Abbott—comes forward and questions him. Prov. 18:17. Abbott questions Centocor's case largely through the testimony of Dr. Brent Iverson. Ex 1071.

Iverson background

Iverson is a Professor in the Department of Chemistry and Biochemistry at the University of Texas. Ex 1071, ¶ 5.

He has been an employee of the University of Texas since 1990. Ex 1071, ¶ 4.

Iverson was awarded a Ph.D. from California Institute of Technology in chemistry in 1987. Ex 1071, Appendix 1, page 11.

While Iverson has worked with antibodies (Ex 1071, ¶ 6), he was not worked with antibodies to human cytokines (Ex 2040, page 15:20-22) (Iverson cross).

IL-12 is a human cytokine. Ex 2015, ¶ 18:5 (O'Neil direct).

Iverson has worked with catalytic antibodies. Ex 2040, page 16:17-18.

Moreover, he says he has "extensive experience" in the field of antibody engineering including development of "novel" antibody engineering technologies and "therapeutic antibodies." Ex 1071, ¶ 8.

Level of skill in the art—Iverson

In Iverson's opinion, a person having ordinary skill the art would have a Ph.D. in molecular biology or "similar degree" as well as at least three years experience working in the field of antibody engineering technology. Ex 1071, ¶ 7.

As becomes apparent, Iverson and O'Neil almost agree, with Iverson requiring only 3 years of experience while O'Neil has a slightly higher 4 year experience requirement.

We are unable to perceive any significant difference between the 3-year and 4-year requirement.

Likewise, we are unable to perceive any significant difference between the degree being in molecular biology (Iverson) or microbiology (O'Neil).

The prior art

Iverson understands Centocor to bottom its obviousness case on information contained in nine "alleged" prior art references. Ex 1071, ¶ 13.

The reason Iverson said "alleged" prior art is that he was wanting to avoid giving an opinion of whether or not the references are legally prior art. Ex 2040, page 51:8-16. Basically, Iverson assumes the references are prior art.

As far as Iverson is concerned, the Abbott claims are not to human antibody to human IL-12. Ex 2040, page 51:19 to page 52:2. At first blush it might seem that Iverson is saying that the Abbott claim cover non-human (possibly chimeric) antibody to human IL-12. Close scrutiny will reveal that

what Iverson means is that the Abbott claims are to human antibody to human IL-20 with "other essential elements." Ex 2040, page 52:3-10.

According to Iverson, none of the nine "alleged" prior art references show all of the essential elements of Abbott's involved claims. Ex 1071, ¶ 14. Iverson recognizes that it is not necessary for a reference to teach all the elements to make out an obviousness case. Ex 2040, page 54:14-18.

Iverson had occasion to consider the definition of "human antibody" in the Abbott patent. Ex 1071, ¶ 15.

What Iverson found was the following (Ex 2010, col. 26:55 to col. 27:14):

> The term "human antibody" includes antibodies having variable and constant regions corresponding to human germline immunoglobulin sequences ... [h]owever, the term "human antibody" ... is not intended to include antibodies in which CDR sequences derived from the germline of another mammalian species, such as a mouse, have been grafted onto human framework sequences.

In other words, "human antibodies" means human not part human and part something else. A chimeric antibody is not an Abbott "human antibody."

According to Iverson, all of the IL-12 references relied on by Centocor refer to research antibody sequences from *non*-humans. Ex 1071, ¶ 16.

Valiante and Trinchieri are said to describe a mouse antibody. Ex 1071, ¶ 16.

Chizzonite and Gately are said to describe a rat antibody. Ex 1071, ¶ 16. The Iverson direct testimony mentions Trinchieri when it should have referred to Gately, a matter cleared up on cross. Ex 2040, page 57:1-2.

According to Iverson, one of ordinary skill in the art in March of 1999 would appreciate the scientific distinction between (1) a non-human antibody sequence and (2) a human antibody sequence based on the species origin of the sequences. Ex 1071, ¶ 17.

Iverson comment on O'Neil definition of "human antibody"

Iverson had an opportunity to comment on the O'Neil definition of "human antibody."

Iverson understands, as do we, that the O'Neil definition of human antibody includes any protein at all so long as there is about 80% sequence identity to some human antibody. Ex 1071, ¶¶ 18-19. Iverson refers to O'Neil's cross at Ex 1089, page 13. There O'Neil says that homogenous sequences would be "ok" (our word) provided there is at least about 80 percent of the sequences are human. Ex 1089, pages 13:5 and 21-23.

In Iverson's view, the O'Neil definition is inconsistent with the general prior art understanding in 1999. A human antibody would be an antibody sequence that originated from a human. Ex 1071, ¶ 22. See also Ex 2040, page 63:9-12:

> I believe the term "human antibody" refers to an antibody [sequence] that is derived from a human as well as derivatives of that sequence in which changes have been made that enhance properties.

Iverson's understanding seems to be consistent with Abbott's definition of "human antibody."

Unlike O'Neil, Iverson says "human antibody" is talking about the source not about what percent of the antibody is human. Ex 2040, page 72:13-19. See also Ex 2040, page 73:6-7. "If the sequence derives from a human, it's a human antibody." Ex 2040, page 77:4-5. "If the sequence of the antibody we're talking about is identical to a human antibody sequence derived from a human, it is a human antibody whether or not there happens to be a coincidental sequence correspondence with another species." Ex 2040, page 78:11-15. Lastly, see Ex 2040, page 116:2-7.

Iverson also explained that it would be unlikely that a human antibody would have one hundred percent identity to a non-human antibody. Ex 2040, page 115:12-15.

Phrase "reasonable expectation of success" and word "therapeutic"

What does the phrase "reasonable expectation of success" mean? It appears that it depends on who you ask and the context.

Both counsel for the parties and the witnesses mention "expectation of success."

There is the "patentese" meaning—the meaning used by patent attorneys, the PTO and the courts—one skilled in the art would reasonably expect success when following the prior art.

There is also another meaning—one used by others, such as scientists.

For a scientist, success can—but does not necessarily—mean achieving a result after a long arduous investigation.

In evaluating testimony of scientists, it may not be a good idea to assume the scientist is using the patentese meaning.

There is another word which is used in various ways in this case.

The word is "therapeutic."

Abbott's claims do not use the word "therapeutic."

As a result, Centocor will criticize testimony which attempts to read the word "therapeutic" into the claims.

On the other hand, what Abbott would say is the K_d and the k_{off} limitations in a practical way are necessary to obtain a "therapeutic" product.

Expectation of success—Iverson's view

Iverson recognizes that O'Neil (or at least Centocor—which bases it case on the O'Neil testimony) believes the prior art would have lead one skilled in the art to believe that if you just follow the recipe you would expect success.

Iverson testified that if one of ordinary skill in the art were to attempt to isolate a potentially *therapeutic* antibody targeted against IL-12 from a repertoire library, due to the stochastic nature of the underlying process there is no reasonable *expectation of success* in obtaining an antibody sequence having the recited characteristics of the antibody sequence corresponding to Abbott's involved claims. Ex 1071, ¶ 26.

Iverson uses the term "therapeutic" to refer to the "characteristics" set out in the Abbott claims. In other words, if the antibody has those characteristics, it is "therapeutic" but if the antibody does not have those characteristics, then it is *not* therapeutic.

Iverson addresses "expectation of success." Ex 1071, ¶¶ 26-27.

According to Iverson, the O'Neil approach ignores the stochastic nature involved in making the known technology yield the affinity matured human antibody sequence with the characteristics (i.e., K_d and k_{off}) recited in Abbott's involved claims. Ex 1071, ¶ 26.

We understand Iverson's reference to "stochastic" to mean that a stochastic process is one whose behavior cannot be precisely determined—

whatever result is obtained may be the result of both predictable action and at least one element which is random.

Further according to Iverson, if the processes described in the "alleged" prior art were to be used to attempt to isolate a potentially therapeutic antibody targeted against IL-12 (an antibody with Abbott's claimed characteristics) from a repertoire library not previously immunologically enriched, the "stochastic" nature of the process "means there is no reasonable expectation of success ..." Ex 1071, ¶ 26.

Numerous problems are said to have been ignored by O'Neil. Ex 1071, ¶ 27.

According to Iverson, in 1999 it was extremely difficult from a technical standpoint to construct highly fertile human sequence repertoire libraries. Ex 1071, ¶ 27.

Iverson says there are at least four factors in creating a useful repertoire library with sufficient diversity to obtain an antibody sequence specific for a given target antigen. Ex 1071, ¶ 27.

First, the PCR [polymerase chain reaction] amplification of antibody repertoire sequences is complicated by the need to use multiple primers to cover a significant portion of the action repertoire. Ex 1071, ¶ 27.

As a result, PCR efficiency is limited, thereby narrowing cloned sequence diversity. Ex 1027, ¶ 27.

A related problem is that it can be difficult to know that all of the appropriate primers are being used to maximize recovery of the antibody sequences from a given natural source. Ex 1071, ¶ 27.

Second, isolated antibody sequences must be used to express folded and active antibody proteins in bacteria. Bacteria are the common host for phage display, not mammalian cells. Ex 1017, ¶ 27, page 8.

A net result may be that many misfolded and therefore non-functional antibodies limit the functional diversity of the library. Ex 1017, ¶ 27, page 8.

Third, cloning heavy and light chain gene sequences independently means that when recombined in a cloned library, any information concerning which heavy chain-light chain combinations are compatible may be lost. Ex 1071, ¶ 27, page 8.

A result is that many phage might produce incompatible combinations thereby limiting functional diversity. Ex 1071, ¶ 27, page 8.

Fourth, each round of library re-growth favors enrichment of phage that propagate the fastest at the expense of more slowing propagating phage. Ex 1071, ¶ 27, page 8.

Enrichment bias can significantly erode library diversity and make it difficult to repeatedly use a given repertoire library. Ex 1071, ¶ 27, page 8.

There was considerable cross-examination on what Iverson means by "reasonable expectation of success." It starts at page 90 of Ex 2040.

Iverson testified that it means "[i]t's not going to work." Ex 2040, page 90:22.

Unsatisfied with that answer, Iverson was asked to be little bit more specific.

Iverson explained: "[t]he underlying process is unpredictable." Ex 2040, page 91:7.

Counsel stated "so you're saying that because it's unpredictable, it's not going to work?"

Iverson further explained: "No. I'm saying it is unpredictable and it's unlikely to work." Ex 2040, page 91:10-11.

"Unlikely to work or unlikely to work at all?" asked counsel.

Iverson answered: "I mean it's—it's unlikely to work at all." Ex 2040, page 92:5.

Counsel came back noting that if it was unlikely to work, "then how do you account for the fact that it has been successfully done prior to 1999 by others?" Ex 2040, page 92:16-18.

The question demonstrates the problem with using the word "it."

Iverson promptly indicated that he was referring to "phase display technology used to isolate antibodies specific to an antigen with no further qualifier." Ex 2040, page 92:19-23.

After some back and forth on other matters, Iverson continued to testify: "I still believe that there's no reasonable expectation of success." Ex 2040, page 96:19-20.

You mean that it is not likely you would be able to do it asked counsel.

Iverson answered: "That is correct." Ex 2040, page 96:25.

Iverson was asked about affinity maturation.

"Affinity maturation is a process by which the affinity of an antibody ... is improved." Ex 2040, page 99:24-25. The reader familiar with our opinion on Abbott Motion 7 will appreciate that improvement of Joe characteristics from Joe 8 to Joe Y61/Joe J695 involved "affinity maturation."

How does one go about improving affinity maturation?

Iverson explained that "[t]he underlying process is inherently unpredictable." Ex 2040, page 100:5-6.

Obtaining affinities (association constants) greater than 10^9 "was difficult." Ex 2040, page 9.

Iverson goes on to say that in 1999 "it is not likely" one would be able to obtain association constants of greater than 10^9. Ex 2040, page 100:15.

Counsel asked, "[w]hen you say that affinity maturation is stochastic, you mean it's a random process; is that right?"

Iverson noted that "[r]andom can mean a lot of things. I mean it's unpredictable." Ex 2040, page 101:6-7.

Later in cross, the following took place (Ex 2040, page 104:3-11) (italics added):

> Q. Okay. So would—would a person skilled in the art in 1999 expect to be able to get an affinity of 10 to the 9th, starting with, let's say, an affinity of 10 to 6th?
>
> A. Understanding that this is *unpredictable*, my opinion is that getting an antibody with an affinity of 10 to 9th, inverse molar, association constant, there is a *reasonable expectation* that that could be obtained.

"10 to 9th, inverse molar" means 10^{-9} or $1/10^9$.

At first blush, it appears that Iverson has contradicted himself. On the one hand, it is unpredictable but on the other hand there is a reasonable expectation of success. What we understand Iverson to be saying is that the field is generally unpredictable, but that ultimately he would have expected that one skilled in the art would have been able to achieve affinities of 10 to the 9th. *Cf.* Ex 2040, page 113:17-20.

Achieving 10 to the 9th is one thing, but achieving 10 to the 10th is another thing.

As Iverson states (Ex 2040, page 105:17-20):

> In—in my experience, in my laboratory, it was very difficult to obtain antibodies approaching 10 to the 10th. We had some

examples where we were better than 10 to the 9th, but they were rare.

HBV and HIV technology

Iverson was of the opinion that O'Neil was of the view that 1992 phage display techniques had been used to generate human antibodies to hepatitis B virus and HIV. Ex 1071, ¶ 29 (Iverson direct); Ex 2015, ¶ 48 (O'Neil direct).

However, in the context of the invention involved in the interference, Iverson believes that O'Neil's view is "misleading" "because it ignores the scientific premise that isolating antibodies to foreign antigen (e.g., HBV and HIV) *is not predictive* for isolating antibodies to self-antigens (e.g., IL-12)."

By using the word "misleading" we understand Iverson not to be accusing O'Neil of any improper motive; rather "misleading" means "mistaken."

In considering ¶ 29 of Iverson's testimony, Iverson noted during cross that he made an error in citing Burton when he meant Zebedee and another error when he cited Zebedee when he meant Burton. Ex 2040, page 106:23.

Iverson agreed that Burton and Zebedee report having isolated antibodies to foreign antigens. Ex 2040, page 108:13-17.

However, Iverson explained that "is not predictive" means that "[o]ne does not follows the other." Ex 2040, page 107:16. We understand "[o]ne does not follows the other" to mean isolating antibodies to self-antigens does not predictably follow from isolation of antibodies to foreign antigens.

Abbott's success

Despite a back and forth on phage technology and a vigorous cross-examination attack attempting to dislodge Iverson from his

"unpredictability" position, counsel for Centocor asked (Ex 2040, page 110:20-21):

> how to you explain that Abbott was able to obtain such a[n] antibody?

In effect, counsel is asking Iverson how was Abbott able to make the claimed invention.

The question is not relevant. Section 103 states that "[p]atentability shall not be negatived by the manner in which the invention was made." The question should never have been asked.

Responding to the irrelevant question, Iverson noted that he was not involved in the Abbott work and noted according to col. 55:66 *et seq.*, Abbott says in its patent that it achieved its result "in the absence of a phage display selection." Ex 2040, page 111: 9-12.

Iverson goes on to say (Ex 2040, page 112:20-23):

> It is an unpredictable process, because we do not understand ahead of time what changes will produce enhanced affinity. I am unaware, as of 1999, that there were procedures that would reliable product [enhanced affinity].

F. Centocor's obviousness case—discussion

1. Differences

In a light most favorable to Centocor, the subject matter of the Abbott claims differs from Trinchieri in that Trinchieri does not describe the K_d and k_{off} limitations in the Abbott claims.

Abbott, of course, maintains that in addition Trinchieri does not describe human antibody to human IL-12. The problem with Trinchieri's position is Trinchieri claim 5: "The antibody of claim wherein said antibody is a human antibody." Even if Trinchieri describes a human antibody,

O'Neil agrees that it is not a neutralizing human antibody. Ex 1089, page 135:4-13 and page 150:9-15.

Other references also differ in that they do not describe human antibodies.

The main difference between any one reference and the Abbott claims, however, is that none describe a human IL-12 antibody with Abbott's K_d or k_{off}. In other words, Abbott's claim require a degree of affinity not described in the prior art for any isolated human antibody that binds to IL-12.

2. Obviousness

Centocor argues that the subject matter of the involved Abbott claims would have been obvious notwithstanding any of these differences.

In Centocor's view, this obviousness case boils down to Abbott using known material and processes for their known purpose to achieve an *expected* result.

It is the "expected result" which gives us pause—and a considerable pause at that.

O'Neil says the subject matter and field are predictable. Iverson says the subject matter and field are *not* predictable. We have a classic—if not to be expected—difference of opinion between well-intended and qualified "experts."

Whether technology is predictable or unpredictable is a question of fact. *Enzo Biochem, Inc. v. Calgene, Inc.*, 188 F.3d 1362, 1372 (Fed. Cir. 1999).

To make a factual finding on unpredictability, we weigh the O'Neil testimony vis-à-vis the Iverson testimony.

To the extent that the O'Neil testimony conflicts with that of Iverson, we credit the Iverson testimony over the O'Neil testimony.

Our credibility determination is based on a consideration of the O'Neil and Iverson direct and cross-examination testimony, as a whole. In particular, we are more impressed with Iverson's explanation of what would have been expected than O'Neil's explanation. Iverson's definition of human antibody more closely comports with the definition in the Abbott patent. While it does not play a major role in our credibility determination, we note that O'Neil is a Centocor employee whereas Iverson is not an Abbott employee. We believe both witnesses have stated honest opinions based on the evidence each considered and their respective experience. They both believe what they are saying is correct. The witnesses simply have an honest disagreement.

As a result of our credibility determination, we find that the technology involved in this case, and in particular the subject matter claimed by Abbott, is generally unpredictable. We also find that one skilled in the art in 1999 would not have had a "reasonable expectation of success" (in the "patentese" sense) based on the prior art relied upon by Centocor.

Try as hard as it might, Centocor cannot fit this case squarely within *KSR*.

One factor to be considered in an obviousness analysis is whether there is a marketplace demand for the invention. *KSR Int'l Co. v. Teleflex, Inc.*, 550 U.S. 398, 418, 127 S. Ct. 1727, 1741 (2007). In this case, we entertain no doubt that there was a market place demand. Stated in other terms, the pharmaceutical industry (and therefore one skilled in the art) was "motivated" to achieve the Abbott invention.

Another factor to be considered is whether prior art elements and techniques were being used by the Abbott inventors for their intended purpose. As a general proposition, we think they were.

Centocor argues that since techniques known to improve one device (chimeric antibodies) those techniques might be used to improve similar devices (non-chimeric human antibodies) in the same way. *KSR*, 550 U.S. at 417, 127 S. Ct. at 1740. *See also In re Sullivan*, 498 F.3d 1345, 1351 (Fed. Cir. 2007) (involving antibodies and rattlesnake venom). We can agree with Centocor that one skilled in the art would have been inclined to use chimeric antibody techniques to make human antibodies.

Where the Centocor obviousness case falls apart is when it comes to predictability. As *KSR* notes, to resolve obviousness one has to ask whether the improvement is more than the predicable use of prior art elements according to their established functions. 550 U.S. at 417, 127 S. Ct. 127 at 1740. What was unpredictable was an expectation of achieving the claimed affinities. In other words, this is a *not* case where one skilled in the art would have had a reasonable expectation of success as urged by Centocor. *Cf. United States v. Adams*, 383 U.S. 39, 51 (1966) (Adams battery produced a result which was shown to have been unexpected) and *Corona Cord Tire Co. v. Dovan Chemical Corp.*, 276 U.S. 358, 368-69 (1928) (the catalytic action of an accelerator cannot be forecast by its chemical composition, for such action is not understood and it not known except by actual test).

We understand what Centocor, through O'Neil, is trying to say. However, with all due respect to her credentials, we think she fell into a hindsight analysis. Now that "the cat is out of the bag", so to speak, and the Abbott invention is "published" via the Abbott patent, a lot of things become

"obvious." Unfortunately for Centocor, the subject matter must have been obvious at the time without the benefit of the Abbott specification. Obviousness is based on prior art which would lead a person skilled in the art to make the claimed invention and reasonably expect success in any endeavor to do so.

Alleged failure of others

A so-called secondary factor relevant to an obvious analysis is unsuccessful attempts by others. According to Abbott, others tried to do what Abbott did but gave up. Unfortunately for Abbott, to establish a failure of others Abbott was under a burden to show that the "others" failed notwithstanding actual knowledge of the art relied upon by Centocor. *Toledo Pressed Steel Co. v. Standard Parts, Inc.*, 307 U.S. 350, 356 (1939). Because, Abbott failed to show that the "others" actually knew of the prior art, we decline to accord any weight to Abbott's failure of other proofs and argument.

G. Order

Upon consideration of Centocor Motion 1 and Abbott Motion 1, and for the reasons given, it is

ORDERED that Centocor Motion 1 is *denied.*

FURTHER ORDERED that Abbott Motion 1 is *denied.*

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(cc via electronic mail)

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